201-14969

RECEIVED
OPPT CBIC
03 DEC 30 PM 3:19

HPV Assessment Report
On
Benzoyl Chloride
CAS No. 98-88-4

December 24, 2003

Benzoates Panel
American Chemistry Council
1300 Wilson Boulevard
Arlington, VA 22209

Contents

1. Introduction

ATOFINA Chemicals, Inc., Bayer Chemicals LLC, and Velsicol Chemical Corporation formed a consortium under the American Chemistry Council (ACC) Benzoates Panel (Panel) to participate in the High Production Volume (HPV) Challenge Program for benzoyl chloride, (CAS 98-88-4). This substance is classified as a high production volume (HPV) chemical according to criteria established by the U.S. EPA, (i.e., > 1,000,000 pounds manufactured or imported into the USA annually).

In consideration of animal welfare concerns to minimize the use of animals in the testing of chemicals, the Panel has conducted a thorough literature search for all available data, published and unpublished, on benzoyl chloride (CAS 98-88-4). It has also performed an analysis of the adequacy of the existing data and is submitting the IUCLID containing (robust) summaries and test plan.

2. Evaluation of SIDS endpoints

In this section, an evaluation of all data available on SIDS endpoints is given.

The substance under consideration is an organic liquid. As it is an acyl chloride it is very reactive towards water, alcohols and amines. In aqueous systems it is almost instantly converted to benzoic acid and hydrogen chloride; even at low pH, the half-life is less than 10 minutes.

2.1. Physico-chemical endpoints

Adequate data on melting point, boiling point, density and vapor pressure are available. Since the substance is a liquid, melting point is not a required endpoint. The partition coefficient and water solubility could not be measured because the substance reacts with water. The log K_{ow} was calculated with EPISuite, but the program indicated that the estimate was questionable due to the fact that acyl halides hydrolyse.

Conclusion: Physico-chemical endpoints have been fulfilled.

Benzoyl chloride CAS 98-88-4				
	Value	**Comment**	**Klimisch Score**	**Reference (See Appendix)**
Melting point (°C)	-1		2	2-5
Boiling point (°C)	197.2		2	2,3,5
Density (g/cm^3)	1.21	at 20°C	2	2,6
Vapor pressure (hPa)	.5	at 20 °C	2	5-6
Partition coefficient (log K_{ow})	1.1	1,2-dichlorobenzene/water	2	7
Water solubility (mg/L)	N.A.	decomposition	2	4-5

N.A. = Not applicable

2.2. Environmental fate

The half-life for reaction of benzoyl chloride with hydroxyl radicals in the atmosphere was estimated to be 2.1 days by EPA's Graphical Exposure Modelling System. Hydrolysis is very fast as already mentioned above. Therefore distribution of this substance over the different compartments is not applicable. The substance is expected to be partitioned to the water compartment and is expected to be hydrolysed before it can reach other compartments. The substance was degraded by 90% within 10 days as measured by biological oxygen demand. Therefore, the substance can be considered readily biodegradable.

Conclusion: Environmental fate endpoints have been fulfilled.

Benzoyl chloride CAS 98-88-4				
	Value	**Comment**	**Klimisch Score**	**Reference (See Appendix)**
Photodegradation (t1/2)	2.1 days		2	10
Hydrolysis (t1/2)	16 sec	pH not mentioned	2	12-14
Distribution in water/air/soil/sediment	N.A.	see hydrolysis		
Ready biodegradability	90% in 10 d		2	15

N.A. = Not applicable

2.3. Ecotoxicity

In a static 96-hour acute fish study with *Pimephales promelas* – predominantly performed according to OECD 203 - an LC50 of 34.1 mg/L was determined. The pH of the test solution at the end of the exposure period had dropped to 5.2 in fresh water, due to decomposition of benzoyl chloride to hydrogen chloride. Also the dissolved oxygen had decreased below the 60% level. A second static test with *Pimephales promelas* resulted in an LC50 of 34.7 mg/L. Two other static tests with *Brachydanio rerio* and *Leuciscus idus* resulted in an LC50 of 7.5 and 200 mg/L, respectively, but analytical monitoring of the system was not done. The overall weight of evidence results in an LC50 of ca. 34 mg/L.

For invertebrates, a static 96-h test with *Palaemonetes pugio* resulted in an LC50 of 180 mg/L. For algal inhibition, no adequate data were located.

Conclusion: Ecotoxicity endpoints for fish and Daphnia have been fulfilled. No adequate data were located for the endpoint, so an algal study (OECD 201) is proposed.

Benzoyl chloride CAS 98-88-4					
	Value	**Species**	**Time of exposure (hr)**	**Klimisch Score**	**Reference (See Appendix)**
Acute fish (LC50, mg/L)	34.1	*Pimephales promelas*	96	2	16
Acute invertebrates (EC50, mg/L)	180	*Palaemonetes pugio*	96	2	16
Algal inhibition (EC50, mg/L)	-				

2.4. Mammalian toxicity

2.4.1. Acute toxicity

In an acute oral study, 6 different doses from 1.0-5.0 ml/kg were administered to male Wistar rats (10 animals/dose). An LD50 of ca. 2,500 mg/kg bw was determined. All animals showed symptoms including sedation, extention spasm and reduced general condition. Macroscopic examination was not performed. Other non-guideline studies with similar values for the LD50 (1,900-2,618 mg/kg bw) are available.

Acute inhalation toxicity was tested in male and female Wistar rats exposed to concentrations of 0.19, 0.50, 0.71, 1.45 and 1.98 mg benzoyl chloride/L for 4 hours. At 1.45 and 1.98 mg/L, 5/10 and 6/10 males as well as 1/10 and 3/10 females died, respectively. Clinical signs included inactivity, piloerection, unkempt fur, and difficulties in breathing up to 19 days post exposure in all rats. Pathological examination of rats that died showed dark red colored lungs with emphysema; some rats showed lung edema. Surviving rats at the two highest exposure levels exhibited lung emphysema with mottled appearance; some showed enlarged adrenals. From the information available, it is concluded that the test is comparable to a guideline study (OECD 403). The LC50 for males and females is ca. 1.45 and >1.98 mg/L, respectively. Two more studies using shorter exposure periods confirmed that the LC50 >2 mg/L.

The LD50 for acute dermal toxicity was determined to be above the limit test value of 2000 mg/kg bw. 2 male and 2 female rabbits were exposed to neat benzoyl chloride. All rabbits exhibited fissuring on the site of application. Benzoyl chloride is expected to react/hydrolyse directly on the site of application; therefore, only systemic effects of benzoic acid would be expected.

Conclusion: Acute toxicity endpoints have been fulfilled.

2.4.2. Genetic toxicity

The test substance was not mutagenic in the Bacterial Reverse Mutation Assay (Ames test) with *Salmonella typhimurium* TA98, TA100, TA1535 and TA1537 strains. Four other reverse mutation tests with *S. typhimurium* strains are available, one of which reported an ambiguous result and one a positive result. Three of four reverse mutation tests with *E. coli* strains were negative. A *Bacillus subtilis* recombination assay was also reported to be negative.

In an *in vivo* micronucleus assay, 0 or 1750 mg/kg bw of benzoyl chloride was administered to mice by gavage. The study was performed under GLP following guideline OECD 474 and showed a negative result.

Conclusion: Genetic Toxicity endpoints have been fulfilled.

2.4.3. Repeated dose toxicity

Adequate data on repeated dose toxicity could not be located.

2.4.4. Reproductive/developmental toxicity

Adequate data on reproductive and developmental toxicity could not be located.

Conclusion (mammalian toxicity): Acute toxicity and genetic toxicity endpoints have been fulfilled. A single OECD 422 (Combined repeated dose toxicity study with the reproductive/developmental toxicity screening test) is proposed.

Benzoyl chloride CAS 98-88-4				
	Value	**Species**	**Klimisch Score**	**Reference (See Appendix)**
Acute toxicity				
Acute oral (LD50, mg/kg)	ca. 2500	Wistar rat	2	4, 20, 21
Acute dermal (LD50, mg/kg)	>2000	New Zealand white rabbit	2	22
Acute inhalation (LC50, mg/m^3)	ca. 1.45	Wistar rat	2	25
Genetic toxicity				
in vitro gene mutation (Ames test)	negative	S. typhimurium TA98, TA100, TA1535 and TA1537	1	30
in vivo (micronucleus)	negative	mouse	1	37
Subacute/Chronic toxicity				
Repro/developmental toxicity	-			

2.5. Data matrix

A table with all data available on SIDS endpoints is presented below.

Benzoyl chloride CAS 98-88-4				
	Value	**Comment/Species**	**Klimisch Score**	**Reference (See Appendix)**
Physicochemical properties				
Melting point (°C)	-1		2	2-5
Boiling point (°C)	197.2		2	2,3,5
Density (g/cm^3)	1.21	at 20°C	2	2,6
Vapor pressure (hPa)	.5	at 20 °C	2	5-6
Partition coefficient (log K_{ow})	1.1	1,2-dichlorobenzene/water	2	7
Water solubility (mg/L)	N.A.	decomposition	2	4-5
Environmental fate				
Photodegradation (t1/2)	2.1 days		2	10
Hydrolysis (t1/2)	16 sec	pH not mentioned	2	12-14
Distribution in water/air/soil/sediment	N.A.	see hydrolysis		
Ready biodegradability	90% in10 d		2	15
Ecotoxicity				
Acute fish (96-h LC50, mg/L)	34.1	*Pimephales promelas*	2	16
Acute invertebrates (96-h EC50, mg/L)	180	*Palaemonetes pugio*	2	16
Algal inhibition (EC50, mg/L)	-			
Mammalian toxicity				
Acute toxicity				
Acute oral (LD50, mg/kg)	ca. 2500	Wistar rat	2	4, 20, 21
Acute dermal (LD50, mg/kg)	>2000	New Zealand white rabbit	2	22
Acute inhalation (LC50, mg/m^3)	ca. 1.45	Wistar rat	2	25
Genetic toxicity				
in vitro gene mutation (Ames test)	negative	S. typhimurium TA98, TA100, TA1535 and TA1537	1	30
Chromosomal aberration	-			
in vivo (micronucleus)	negative	mouse	1	37
Subacute/Chronic toxicity				
Repro/developmental toxicity	-			

N.A. = Not applicable

3. Data availability and testing proposal

The availability of data is depicted in the following table.

	Benzoyl chloride CAS 98-88-4
Physico-chemical	
Melting point	+
Boiling point	+
Density	+
Vapor Pressure	+
Partition Coefficient	N.A.
Water Solubility	N.A.
Environmental Fate	
Photodegradation	+
Hydrolysis	+
Distribution in compartments	N.A.
Ready Biodegradability	+
Ecotoxicity	
96-h LC50 Fish	+
48-h EC50 Daphnia	+
72-h EC50 Algal Inhibition	OECD201
Mammalian toxicity	
Acute toxicity	+
Repeated Dose Toxicity	OECD422
Genetic Toxicity	+
Reproductive/Developmental Toxicity	OECD422

+ = data available
N.A. = not applicable
OECD = test to be performed

4. REFERENCES

(From IUCLID Data Set for Benzoyl Chloride in Appendix)

(1) ACGIH. 2002. TLVs and BEIs

(2) CRC Handbook of Chemistry and Physics. 1999. David R. Lide, ed. CRC Press, New York. p 3-80, #2886.

(3) Handbook of Environmental Data of Organic Chemicals. 2nd edition. 1983.

(4) Safety Data Sheet. ELF ATOCHEM, UK. December, 1992

(5) Verscheuren K. 1983. Handbook of Environmental Data of Organic Chemicals. Second edition. p. 282

(6) Auer-Technikum, Auerges. mbH Berlin, 12. Ausg. 1988

(7) Great Lakes Chemical Corporation. 04/25/78. Partition coefficients of several flame retardants and industrial chemicals. TSCA 8(d) submission. TSCATS Microfiche No. 206828.

(8) Bayer AG data

(9) Syracuse Research Corporation calculated values, 1988.

(10) USEPA. 1985. GEMS: Graphical Exposure Modelling System. Fate of atmospheric pollutants data base. Office of toxic substances.

(11) Shashidhar M.A., 1971. Electronic absorption spectra of some monosubstituted benzenes in the vapour phase. Spectrochemica Acta. 27A:2363-2372.

(12) Mabey W. and Mill T. 1978. Critical review of hydrolysis of organic compounds in water under environmental conditions. J. Phys. Chem. Ref. Data. 7:383-415.

(13) Morrisson R.T. and BOYD R.N. 1973. Organic Chemistry.

(14) Meylan W. and Howard P. 1999. EPIWin Modeling Program. Syracuse Research Corporation. Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212-2510.

(15) Bayer AG data, OC-P/Ökologie Study BSB-No 213, 1974-04-19

(16) Curtis M.W. and Ward C.H. 1981. J. Hydrol. 51:359-367

(17) Bruns, Mueller, Caspers. 2001. Institute of Environmental Analysis and Evaluation. Bayer AG study.

(18) Curtis M.W. et al. 1979. Water Research 13:137-141.

(19) Kaiser K.L.E. et al. 1987. QSAR Environ. Toxicol. "Proc. Int. Workshop, 2nd Meeting Date 1986". Edited by: Kaiser K.L.E., Reidel, Dordrecht, Neth. pps.153-168.

(20) Bayer AG data, Loeser E., 1978. Akute orale Toxizität, short report, November/03/1978

(21) Loeser E. 1978. Bayer AG data, short report, November/03/1978.

(22) Velsicol Chem Corp. 1974. Acute toxicity studies in rats and rabbits. EPA-OTS0107. Report # 163-281.

(23) ITII, International Technical Information Institute, Tokyo, Japan. 1975. Cited in Chemical Hazard Information Profile (CHIP) Benzoyl Chloride, draft report, 1982.

(24) Izmerov N.F. et al. 1982. Toxicometric parameters of industrial toxic chemicals under single exposure. Centre of International Projects, GKNT, Moscow, p. 25.

(25) Bayer AG data, Report No. 8418, Benzoylchlorid, gewerbetoxikologische Untersuchungen, June/01/1979

(26) Yoshimura H. et al. 1986. Sangyo Igaku (Jpn.J.Ind.Health) 28:352-359

(27) Fukuda K. 1981. Ochanomizu Igaku Zasshi 29:69-81

(28) Fukuda K. et al. 1981. GANN 72:655-664

(29) Aw T.C., Boyland E. 1981. IRCS Med. Sci: Libr. Compend. 9: 29-30.

(30) Bayer AG data. Report No 17635. January/23/1989. Benzoylchloride: Salmonella /Microsome test to evaluate for point mutagenic effects, preincubation method. (at the request of BG Chemie)

(31) Velsicol Chem Corp. 1980. Mutagenicity evaluation of benzoylchloride in the Ames Salmonella/microsome plate test. EPA-OTS0107.

(32) Chiu CH. W. et al. 1978. Mutat. Res. 58:11-22.

(33) Kawazoe Y. and Kato M. 1982. GANN 73:255-263

(34) McMahon R.E. et al. 1979. Cancer Res. 39:682-693.

(35) Yasuo K. et al. 1978. Mutat. Res. 58:143-150.

(36) Ohkubo T. et al. 1996. Jap. J. Environm. Chem. 6:533-540.

(37) Bayer AG data. Report No. 17383. November/11/1988. Benzoylchloride: Micronucleus test on the mouse to evaluate for clastogenic effects, (at the request of BG Chemie)

(38) Yoshimura H. et al. 1979, cited in Chemical Hazard Information Profile (CHIP) Benzoyl Chloride, draft report, 1982

(39) Tokimoto K. et al. 1978, cited in Chemical Hazard Information Profile (CHIP) Benzoyl Chloride, draft report, 1982.

(40) Sakabe H. et al. 1976. Ann. NY Acad. Sci. 171:67-70

(41) Sorahan T. et al. 1983. Ann. Occup. Hyg. 27:173-182

(42) Sorahan T., Cathcart M. 1989. Br. H. Indust.Med. 46:425-427

(43) Wong O. 1988. Am. J. Indust. Med. 14:417-431

(44) Sakabe H. and Fukuda K. 1977. Ind. Health 15:173-174

(45) Sakabe H. et al., Ann. NY Acad. Sci. 171, 67-70 (1976)

(46) Awogi T. et al. 1986. Mutat. Res. 164:263

(47) Fraga C.G. et al. 1987. Free Radical Biol. Med. 3:119-123

(48) Bayer AG data, Report No. 8418, June/01/1979

(49) Wang P.Y. and Evans D.W. 1977. Biomed. Med. Dev. Art. Org. 5:277-291

APPENDIX

IUCLID Data Set for Benzoyl Chloride